Subject Search J. Hines; 09/756,071

Point of Contact:
Thomas G. Larson, Ph.D.
703-308-7309
CM1, Rm. 6B01

```
=> FILE CANCERLIT
FILE 'CANCERLIT' ENTERED AT 16:38:32 ON 11 JUN 2002

 FILE COVERS 1963 TO 14 Jun 2001 (20010614/ED)

 CANCERLIT thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2000 vocabulary.  Enter HELP THESAURUS for details.

 This file contains CAS Registry Numbers for easy and accurate substance
 identification.
```

PFT = Preferred or forbidden term

NT = Narrower Terms

```
=> D QUE L27
L14          2483 SEA FILE=CANCERLIT ABB=ON  PLU=ON  LAMININ+PFT/CT
L15         20482 SEA FILE=CANCERLIT ABB=ON  PLU=ON  CELL ADHESION MOLECULES+PFT/
                  CT
L16         22764 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L14 OR L15
L17           164 SEA FILE=CANCERLIT ABB=ON  PLU=ON  KALININ OR LAMININ-5
L20         95352 SEA FILE=CANCERLIT ABB=ON  PLU=ON  ANTIBODIES+NT,PFT/CT
L23           503 SEA FILE=CANCERLIT ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L25           137 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L16 AND L17
L26            27 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L25 AND L20
L27             4 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L26 AND L23


=> D QUE L31
L14          2483 SEA FILE=CANCERLIT ABB=ON  PLU=ON  LAMININ+PFT/CT
L15         20482 SEA FILE=CANCERLIT ABB=ON  PLU=ON  CELL ADHESION MOLECULES+PFT/
                  CT
L16         22764 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L14 OR L15
L17           164 SEA FILE=CANCERLIT ABB=ON  PLU=ON  KALININ OR LAMININ-5
L29         49574 SEA FILE=CANCERLIT ABB=ON  PLU=ON  NEOPLASM METASTASIS+NT,PFT/C
                  T
L30          1893 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L16 AND L29
L31             2 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L30 AND L17


=> D QUE L33
L14          2483 SEA FILE=CANCERLIT ABB=ON  PLU=ON  LAMININ+PFT/CT
L15         20482 SEA FILE=CANCERLIT ABB=ON  PLU=ON  CELL ADHESION MOLECULES+PFT/
                  CT
L16         22764 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L14 OR L15
L17           164 SEA FILE=CANCERLIT ABB=ON  PLU=ON  KALININ OR LAMININ-5
L23           503 SEA FILE=CANCERLIT ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L24             7 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L17 (2W) L23
L33             7 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L16 AND L24


=> D QUE L34
L14          2483 SEA FILE=CANCERLIT ABB=ON  PLU=ON  LAMININ+PFT/CT
L15         20482 SEA FILE=CANCERLIT ABB=ON  PLU=ON  CELL ADHESION MOLECULES+PFT/
                  CT
L16         22764 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L14 OR L15
L17           164 SEA FILE=CANCERLIT ABB=ON  PLU=ON  KALININ OR LAMININ-5
L20         95352 SEA FILE=CANCERLIT ABB=ON  PLU=ON  ANTIBODIES+NT,PFT/CT
L23           503 SEA FILE=CANCERLIT ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L24             7 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L17 (2W) L23
L33             7 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L16 AND L24
L34             0 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L33 AND L20
```

Searched by Thom Larson, STIC, 308-7309

```
=> D QUE L35
L14         2483 SEA FILE=CANCERLIT ABB=ON  PLU=ON  LAMININ+PFT/CT
L15        20482 SEA FILE=CANCERLIT ABB=ON  PLU=ON  CELL ADHESION MOLECULES+PFT/
                 CT
L16        22764 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L14 OR L15
L17          164 SEA FILE=CANCERLIT ABB=ON  PLU=ON  KALININ OR LAMININ-5
L23          503 SEA FILE=CANCERLIT ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L24            7 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L17 (2W) L23
L29        49574 SEA FILE=CANCERLIT ABB=ON  PLU=ON  NEOPLASM METASTASIS+NT,PFT/C
                 T
L33            7 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L16 AND L24
L35            0 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L33 AND L29


=> D QUE L37
L14         2483 SEA FILE=CANCERLIT ABB=ON  PLU=ON  LAMININ+PFT/CT
L15        20482 SEA FILE=CANCERLIT ABB=ON  PLU=ON  CELL ADHESION MOLECULES+PFT/
                 CT
L16        22764 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L14 OR L15
L17          164 SEA FILE=CANCERLIT ABB=ON  PLU=ON  KALININ OR LAMININ-5
L20        95352 SEA FILE=CANCERLIT ABB=ON  PLU=ON  ANTIBODIES+NT,PFT/CT
L23          503 SEA FILE=CANCERLIT ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L25          137 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L16 AND L17
L26           27 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L25 AND L20
L27            4 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L26 AND L23
L36       970090 SEA FILE=CANCERLIT ABB=ON  PLU=ON  NEOPLASMS+NT,PFT/CT
L37            3 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L36 AND L27


=> D QUE L38
L14         2483 SEA FILE=CANCERLIT ABB=ON  PLU=ON  LAMININ+PFT/CT
L15        20482 SEA FILE=CANCERLIT ABB=ON  PLU=ON  CELL ADHESION MOLECULES+PFT/
                 CT
L16        22764 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L14 OR L15
L17          164 SEA FILE=CANCERLIT ABB=ON  PLU=ON  KALININ OR LAMININ-5
L20        95352 SEA FILE=CANCERLIT ABB=ON  PLU=ON  ANTIBODIES+NT,PFT/CT
L23          503 SEA FILE=CANCERLIT ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L24            7 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L17 (2W) L23
L25          137 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L16 AND L17
L26           27 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L25 AND L20
L27            4 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L26 AND L23
L33            7 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L16 AND L24
L36       970090 SEA FILE=CANCERLIT ABB=ON  PLU=ON  NEOPLASMS+NT,PFT/CT
L37            3 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L36 AND L27
L38            0 SEA FILE=CANCERLIT ABB=ON  PLU=ON  L33 AND L37


=> S L27 OR L31 OR L33 OR L37
L99           13 L27 OR L31 OR L33 OR L37

=> FILE BIOTECHNO
FILE 'BIOTECHNO' ENTERED AT 16:40:05 ON 11 JUN 2002
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FILE LAST UPDATED: 04 JUN 2002      <20020604/UP>
FILE COVERS 1980 TO DATE.

>>>  SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN
     /CT AND BASIC INDEX  <<<
```

Carcinoma+NT, PFT

Searched by Thom Larson, STIC, 308-7309

```
=> D QUE L83
L78        4055 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  KALININ OR LAMININ OR
                LAMININ (W) 5
L79          84 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  L78 (5A) (GAMMA2 OR GAMMA
                (W) 2)
L80       31317 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  METASTAS? OR INVAS? OR
                INVAD?
L81          22 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  L79 AND L80
L82      222082 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  ANTIBODY OR IMMUNOGLOBULIN
L83           3 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  L81 AND L82


=> D QUE L86
L78        4055 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  KALININ OR LAMININ OR
                LAMININ (W) 5
L79          84 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  L78 (5A) (GAMMA2 OR GAMMA
                (W) 2)
L82      222082 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  ANTIBODY OR IMMUNOGLOBULIN
L84      180047 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  NEOPLASM OR CANCER OR
                SARCOMA OR TUMOR
L85          26 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  L79 AND L84
L86           6 SEA FILE=BIOTECHNO ABB=ON  PLU=ON  L85 AND L82


=> S L83 OR L86
L100          7 L83 OR L86

=> FILE EMBASE
FILE 'EMBASE' ENTERED AT 16:41:14 ON 11 JUN 2002
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 FILE COVERS 1974 TO 6 Jun 2002 (20020606/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

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=> D QUE L56
L40         332 SEA FILE=EMBASE ABB=ON  PLU=ON  KALININ+PFT/CT
L41        2856 SEA FILE=EMBASE ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L43         188 SEA FILE=EMBASE ABB=ON  PLU=ON  L40/MAJ
L47     1060973 SEA FILE=EMBASE ABB=ON  PLU=ON  NEOPLASM+NT,PFT/CT
L49       95033 SEA FILE=EMBASE ABB=ON  PLU=ON  METASTASIS+NT,PFT/CT
L54          63 SEA FILE=EMBASE ABB=ON  PLU=ON  L43 AND L47
L55          16 SEA FILE=EMBASE ABB=ON  PLU=ON  L54 AND L49
L56           9 SEA FILE=EMBASE ABB=ON  PLU=ON  L55 AND L41


=> D QUE L66
L40         332 SEA FILE=EMBASE ABB=ON  PLU=ON  KALININ+PFT/CT
L41        2856 SEA FILE=EMBASE ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L47     1060973 SEA FILE=EMBASE ABB=ON  PLU=ON  NEOPLASM+NT,PFT/CT
L62      142603 SEA FILE=EMBASE ABB=ON  PLU=ON  L47 (L) (DT OR TH)/CT
L65           1 SEA FILE=EMBASE ABB=ON  PLU=ON  L40 AND L62
L66           0 SEA FILE=EMBASE ABB=ON  PLU=ON  L65 AND L41


=> D QUE L67
```

DT = Drug Therapy
TH = Therapy

```
L40          332 SEA FILE=EMBASE ABB=ON  PLU=ON  KALININ+PFT/CT
L45        13622 SEA FILE=EMBASE ABB=ON  PLU=ON  CANCER INVASION+PFT/CT
L60          216 SEA FILE=EMBASE ABB=ON  PLU=ON  L45 (L) (DT OR TH)/CT
L67            0 SEA FILE=EMBASE ABB=ON  PLU=ON  L40 AND L60


=> D QUE L69
L40          332 SEA FILE=EMBASE ABB=ON  PLU=ON  KALININ+PFT/CT
L49        95033 SEA FILE=EMBASE ABB=ON  PLU=ON  METASTASIS+NT,PFT/CT
L68        10310 SEA FILE=EMBASE ABB=ON  PLU=ON  L49 (L) (DT OR TH)/CT
L69            0 SEA FILE=EMBASE ABB=ON  PLU=ON  L40 AND L68


=> D QUE L73
L40          332 SEA FILE=EMBASE ABB=ON  PLU=ON  KALININ+PFT/CT
L41         2856 SEA FILE=EMBASE ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L47      1060973 SEA FILE=EMBASE ABB=ON  PLU=ON  NEOPLASM+NT,PFT/CT
L70       251930 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIBODY+NT,PFT/CT
L71           78 SEA FILE=EMBASE ABB=ON  PLU=ON  L40 AND L70
L72           21 SEA FILE=EMBASE ABB=ON  PLU=ON  L71 AND L41
L73            5 SEA FILE=EMBASE ABB=ON  PLU=ON  L72 AND L47


=> D QUE L74
L40          332 SEA FILE=EMBASE ABB=ON  PLU=ON  KALININ+PFT/CT
L41         2856 SEA FILE=EMBASE ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L49        95033 SEA FILE=EMBASE ABB=ON  PLU=ON  METASTASIS+NT,PFT/CT
L70       251930 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIBODY+NT,PFT/CT
L71           78 SEA FILE=EMBASE ABB=ON  PLU=ON  L40 AND L70
L72           21 SEA FILE=EMBASE ABB=ON  PLU=ON  L71 AND L41
L74            2 SEA FILE=EMBASE ABB=ON  PLU=ON  L72 AND L49


=> D QUE L75
L40          332 SEA FILE=EMBASE ABB=ON  PLU=ON  KALININ+PFT/CT
L41         2856 SEA FILE=EMBASE ABB=ON  PLU=ON  GAMMA2 OR GAMMA (W) 2
L45        13622 SEA FILE=EMBASE ABB=ON  PLU=ON  CANCER INVASION+PFT/CT
L70       251930 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTIBODY+NT,PFT/CT
L71           78 SEA FILE=EMBASE ABB=ON  PLU=ON  L40 AND L70
L72           21 SEA FILE=EMBASE ABB=ON  PLU=ON  L71 AND L41
L75            2 SEA FILE=EMBASE ABB=ON  PLU=ON  L72 AND L45


=> S L56 OR L73 OR L74 OR L75
L101          12 L56 OR L73 OR L74 OR L75

=> FILE HCAPLUS
FILE 'HCAPLUS' ENTERED AT 16:42:56 ON 11 JUN 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 11 Jun 2002 VOL 136 ISS 24
FILE LAST UPDATED: 9 Jun 2002 (20020609/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> D QUE L6
L2          4872 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "NEOPLASM (L) METASTASIS"+PFT/
                 CT
L3          6416 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LAMININS+NT,PFT/CT
L4           407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 (L) 5
L5            42 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 (L) (GAMMA (W) 2)
L6             0 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 AND L2


=> D QUE L7
L1        195441 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NEOPLASM+NT,PFT/CT
L3          6416 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LAMININS+NT,PFT/CT
L4           407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 (L) 5
L5            42 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 (L) (GAMMA (W) 2)
L7             5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 AND L1


=> D QUE L9
L3          6416 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LAMININS+NT,PFT/CT
L4           407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 (L) 5
L5            42 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 (L) (GAMMA (W) 2)
L8        192393 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIBODIES+NT,PFT/CT
L9             6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 AND L8


=> D QUE L13
L3          6416 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LAMININS+NT,PFT/CT
L4           407 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 (L) 5
L5            42 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 (L) (GAMMA (W) 2)
L12       138843 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTITUMOR AGENTS+NT,PFT/CT
L13            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 AND L12


=> S L6 OR L7 OR L9 OR L13
L102           7 L6 OR L7 OR L9 OR L13

=> FILE WPIDS
FILE 'WPIDS' ENTERED AT 16:44:09 ON 11 JUN 2002
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FILE LAST UPDATED: 10 JUN 2002              <20020610/UP>
MOST RECENT DERWENT UPDATE          200236   <200236/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been
    enabled in WPINDEX/WPIDS and WPIX  >>>
```

Searched by Thom Larson, STIC, 308-7309

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>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX TOOLS OF THE
    TRADE USER GUIDE, PLEASE VISIT:
    http://www.derwent.com/data/stn3.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<

=> D QUE L90
L89          408 SEA FILE=WPIDS ABB=ON  PLU=ON  KALININ OR LAMININ OR LAMININ
                 (W) 5
L90            4 SEA FILE=WPIDS ABB=ON  PLU=ON  L89 (5A) (GAMMA2 OR GAMMA  (W)
                 2)


=> D QUE L94
L89          408 SEA FILE=WPIDS ABB=ON  PLU=ON  KALININ OR LAMININ OR LAMININ
                 (W) 5
L93        48284 SEA FILE=WPIDS ABB=ON  PLU=ON  ANTIBODY OR IMMUNOGLOBULIN
L94            2 SEA FILE=WPIDS ABB=ON  PLU=ON  L93 AND L89 AND (GAMMA2 OR
                 GAMMA (W) 2)


=> D QUE L96
L89          408 SEA FILE=WPIDS ABB=ON  PLU=ON  KALININ OR LAMININ OR LAMININ
                 (W) 5
L95        15859 SEA FILE=WPIDS ABB=ON  PLU=ON  METASTAS? OR INVAS? OR INVAD?
L96            1 SEA FILE=WPIDS ABB=ON  PLU=ON  L95 AND L89 AND (GAMMA2 OR
                 GAMMA (W) 2)


=> D QUE L98
L89          408 SEA FILE=WPIDS ABB=ON  PLU=ON  KALININ OR LAMININ OR LAMININ
                 (W) 5
L97        44597 SEA FILE=WPIDS ABB=ON  PLU=ON  NEOPLASM OR CANCER OR SARCOMA
                 OR TUMOR
L98            1 SEA FILE=WPIDS ABB=ON  PLU=ON  L97 AND L89 AND (GAMMA2 OR
                 GAMMA (W) 2)


=> S L90 OR L94 OR L96 OR L98
L103           4 L90 OR L94 OR L96 OR L98

=> DUP REM L99-L103
FILE 'CANCERLIT' ENTERED AT 16:45:45 ON 11 JUN 2002

FILE 'BIOTECHNO' ENTERED AT 16:45:45 ON 11 JUN 2002
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FILE 'EMBASE' ENTERED AT 16:45:45 ON 11 JUN 2002
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FILE 'HCAPLUS' ENTERED AT 16:45:45 ON 11 JUN 2002
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FILE 'WPIDS' ENTERED AT 16:45:45 ON 11 JUN 2002

PROCESSING COMPLETED FOR L99
PROCESSING COMPLETED FOR L100
PROCESSING COMPLETED FOR L101
PROCESSING COMPLETED FOR L102
PROCESSING COMPLETED FOR L103
L104 38 DUP REM L99-L103 (5 DUPLICATES REMOVED)

=> D IBIB AB 1-38

L104 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:332666 HCAPLUS
DOCUMENT NUMBER: 136:337357
TITLE: Laminin chains: diagnostic uses
INVENTOR(S): Tryggvason, Karl; Kallunki, Pekka; Pyke, Charles
PATENT ASSIGNEE(S): Finland
SOURCE: U.S. Pat. Appl. Publ., 51 pp., Cont.-in-part of U.S. Ser. No. 663,147.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002052307	A1	20020502	US 2001-756071	20010108
US 5660982	A	19970826	US 1994-317450	19941004
US 6143505	A	20001107	US 1997-800593	19970218

PRIORITY APPLN. INFO.:
US 1994-317450 A3 19941004
US 1997-800593 A1 19970218
US 2000-175005P P 20000107
US 2000-663147 A2 20000915

AB The invention concerns the identification, diagnosis, monitoring, and treatment of invasive cells using the laminin 5 gamma-2 chain protein or nucleic acid sequence, or antibodies thereto.

L104 ANSWER 2 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002108996 EMBASE
TITLE: Cytoplasmic expression of laminin .**gamma**. **2** chain correlates with postoperative hepatic metastasis and poor prognosis in patients with pancreatic ductal adenocarcinoma.
AUTHOR: Takahashi S.; Hasebe T.; Oda T.; Sasaki S.; Kinoshita T.; Konishi M.; Ochiai T.; Ochiai A.
CORPORATE SOURCE: Dr. A. Ochiai, Pathology Division, Natl. Cancer Ctr. Research Institute, East, 6-5-1 Kashiwanoha, Kashiwa, Chiba 277-8577, Japan. aochiai@east.ncc.go.jp
SOURCE: Cancer, (15 Mar 2002) 94/6 (1894-1901).
Refs: 31
ISSN: 0008-543X CODEN: CANCAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English

AB BACKGROUND. The laminin .**gamma**.2 chain is involved in tumor invasion and metastasis, but the significance of laminin .**gamma**.2 chain expression remains unclear in patients with pancreatic carcinoma. METHODS. Laminin .**gamma**.2 chain expression was examined immunohistochemically in 48 patients with pancreatic ductal adenocarcinoma who were followed closely to elucidate the correlations between clinicopathologic factors, postoperative recurrence, and overall survival. Prognostic factors for postoperative survival were examined comparing clinicopathologic factors and laminin .**gamma**.2 chain expression. RESULTS. Two different staining patterns of laminin .**gamma**.2 chain expression, cytoplasmic expression and basement membrane expression, were detected in tumors from all 48 patients. Tumors were then classified into two types according to the dominant pattern of laminin .**gamma**.2 chain expression: the cytoplasmic expression dominant type (CYT; n = 26 patients) and the basement membrane expression dominant type (BM; n = 22 patients). Tumor differentiation was associated statistically with the BM type of laminin .**gamma**.2 chain expression (P = 0.0002). The CYT type of laminin .**gamma**.2 chain expression was associated significantly with the occurrence of postoperative hepatic metastasis (P = 0.0011) and also was the strongest predictive factor for poorer overall survival in patients with pancreatic ductal adenocarcinomas (P = 0.0161). CONCLUSIONS. The cytoplasmic expression of the laminin .**gamma**.2 chain represents the high invasive potential of the tumor and is correlated with distant metastasis, especially hepatic metastasis, and with a poorer prognosis in patients with pancreatic ductal adenocarcinoma. .COPYRGT. 2002 American Cancer Society.

L104 ANSWER 3 OF 38 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2002:34001718 BIOTECHNO
TITLE: Epidermal growth factor receptor gene amplification is correlated with **laminin-5** .**gamma**.2 chain expression in oral squamous cell carcinoma cell lines
AUTHOR: Ono Y.; Nakanishi Y.; Gotoh M.; Sakamoto M.; Hirohashi S.
CORPORATE SOURCE: S. Hirohashi, Pathology Division, Natl. Cancer Ctr. Research Institute, 1-1, Tsukiji 5-chome, Chuo-ku, Tokyo 104-0045, Japan.
E-mail: shirohas@gan2.ncc.go.jp
SOURCE: Cancer Letters, (25 JAN 2002), 175/2 (197-204), 34 reference(s)
CODEN: CALEDQ ISSN: 0304-3835
PUBLISHER ITEM IDENT.: S0304383501006826
DOCUMENT TYPE: Journal; Article
COUNTRY: Ireland
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Both epidermal growth factor receptor (EGFR) gene amplification and **laminin** (Ln)-5 .**gamma**.2 chain overexpression have been reported to be poor prognostic factors in patients with squamous cell carcinoma (SCC) of the head and neck. Here we report our investigation of the relationship between EGFR gene amplification and Ln-5 .gamma.2 chain expression in seven SCC cell lines, since both epidermal growth factor (EGF) signaling and Ln-5 .gamma.2 have been reported to be involved in cell motility. The degree of correlation between EGFR gene amplification and Ln-5 .gamma.2 chain expression was evaluated by Southern and Western blot analyses. EGFR gene amplification was detected in all SCC cell lines at levels 5-50 times those in DNA from

normal liver tissue. EGFR gene amplification increased with Ln-5 .gamma.2 chain protein expression in seven cell lines, showing close correlation between EGFR gene amplification and Ln-5 .gamma.2 chain protein expression. In order to show the causal relationship, we analyzed the effects of transforming growth factor-.alpha. (TGF-.alpha.), tyrosine kinase inhibitor of EGFR, and neutralizing **antibody** against EGFR, on the expression of Ln-5 .gamma.2 in these cell lines. In two cell lines in which EGFR gene amplification was low, expression of both protein and mRNA of the Ln-5 .gamma.2 chain increased in the presence of TGF-.alpha., and Ln-5 .gamma.2 chain expression was inhibited by neutralizing **antibody** against EGFR. In all cell lines, Ln-5 .gamma.2 chain expression was inhibited by tyrosine kinase inhibitor which acts selectively on the EGFR signal transduction pathway under the stimulus of TGF-.alpha.. These results suggest that EGFR gene amplification and the EGFR signaling pathway can act as positive regulators on the induction of the Ln-5 .gamma.2 chain secreted by **tumor** cells. .COPYRGT. 2002 Elsevier Science Ireland Ltd. All rights reserved.

L104 ANSWER 4 OF 38 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-089823 [12] WPIDS
DOC. NO. CPI: C2002-027679
TITLE: Regulating **laminin 5** expression or activity for treating squamous cell carcinoma, glioma, by contacting **laminin 5** with an agent that affects processing of **laminin 5** by a bone morphogenetic protein-1 related protein.
DERWENT CLASS: B04 D16
INVENTOR(S): FINDELL, P R; MARINKOVICH, M P
PATENT ASSIGNEE(S): (FIBR-N) FIBROGEN INC; (STRD) UNIV LELAND STANFORD JUNIOR
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001087239	A2	20011122	(200212)*	EN	102

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001061519 A 20011126 (200222)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001087239	A2	WO 2001-US15417	20010511
AU 2001061519	A	AU 2001-61519	20010511

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001061519	A	Based on	WO 200187239

PRIORITY APPLN. INFO: US 2000-203708P 20000512
AB WO 200187239 A UPAB: 20020221
NOVELTY - Regulating (M1) **laminin 5** expression or

activity, comprising contacting **laminin 5** with an agent (A) that affects processing of **laminin 5** by a bone morphogenetic protein-1 (BMP-1) related protein, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition for treating a condition associated with increased expression or activity of **laminin 5**, comprising (A);

(2) diagnosing (M2) the presence of a condition characterized by increased expression or activity of **laminin 5** in a subject, comprising:

(a) obtaining a sample;

(b) detecting the level of expression or activity of a BMP-1 related protein in the sample; and

(c) comparing the level of expression or activity of the BMP-1 related protein in the sample to a standard level of expression or activity of the BMP-1 related protein;

(3) a diagnostic kit for use in diagnosing the presence of a condition associated with increased expression or activity of **laminin 5** in a sample from a subject, comprising an anti-BMP-1 **antibody** reactive with BMP-1 related proteins and a labeled reagent capable of forming a complex with a BMP-1 related protein or with the anti-BMP-1 **antibody**

(4) screening for an agent that affects the processing of **laminin 5** by BMP-1 related proteins, by contacting a sample containing unprocessed **laminin 5** with BMP related protein and the agent, measuring and comparing the level of processed **laminin 5** in the sample to a control sample;

(5) an isolated polypeptide (I) comprising a BMP-1 cleavage sequence (S2);

(6) an isolated polypeptide comprising a BMP-1 cleavage sequence chosen from (S1);

(7) an isolated polynucleotide encoding (I);

(8) an isolated polynucleotide that is complement to the polynucleotide of (7); and

(9) an **antibody** (II) that binds to (I).

S1 is LeuGlnPheGlyAspIleProThr, GlnLeuLeuGlnAspThrProValAla, LysValTrpGlnAspAlaCysSer and GlnPheAlaValAspMetGlnThr. S2 is CysTyrSerGlyAspGluAsnPro.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Inhibitor of processing of **laminin 5** by a BMP-1 related protein.

The processing of **laminin 5** by various BMP-1 related proteins was examined. Unprocessed **laminin 5** was deposited onto the surface of culture dishes by keratinocytes cultured in the presence of 10 micro M inhibitor of BMP-1 activity, which prevented processing of **laminin 5**. The cells were removed from the culture dish by 20 mM ammonium sulfate, the dish was washed, and the matrix was incubated in increasing amounts of each BMP-1 related protein. After proteolytic digestion, the matrix was extracted and examined by Western blot analysis. The results showed that BMP-1, mTld, mTll-1, and mTll-2 processed **laminin 5**. BMP-1, mTld, mTll-1 and mTll-2 all cleaved the alpha 3 chain of **laminin 5**. BMP-1 and mTll-2 cleaved the **gamma 2** chain of **laminin 5**. Additionally, mTll-2 showed more potent cleavage activity towards the alpha 3 chain and **gamma 2** chain of **laminin 5** compared to the other BMP-1 related proteins. The inhibitor at 10 micro M inhibited cleavage of **laminin 5 gamma 2** chain by BMP-1 and mTll-2, and inhibited cleavage of **laminin 5** alpha 3 chain by BMP-1, mTll-1, and mTll-2.

USE - (M1) is useful for affecting **laminin 5** expression or activity, for treating a condition characterized by increased expression or activity of **laminin 5**, especially **cancer**, glioma, a condition characterized by neoplastic epithelial cells chosen from squamous cells, keratinocytes, mucosal epithelial cells, gastrointestinal epithelial cells, corneal epithelia of the eye and epithelial cells of the urinary and reproductive tract, squamous cell carcinoma such as **cancers** of the skin, lung, head, neck, oral, cervical, tongue, gastric, colorectal, throat, **cancer** of the urinary tract, reproductive tract, esophageal **cancer** and bronchiogenic carcinoma. (M2) is useful for diagnosing the presence of squamous cell carcinoma in a subject by detecting the level of expression of BMP-1 related protein in tissue, urine, serum or blood sample. (I) is useful for screening for an agent that affects the processing of **laminin 5** by BMP-1 related proteins by contacting sample containing the polypeptide with a BMP-1 related protein and an agent, measuring and comparing the level of the polypeptide that is processed in the sample to a control sample. (All claimed). (II) is useful to identify BMP-1 related proteins, **laminin 5** or processed **laminin 5** or **laminin 5** chains, or their fragments or subunits, in a sample e.g. from biopsied tissue, and to inhibit processing of **laminin 5** by BMP-1 related proteins.
Dwg.0/26

L104 ANSWER 5 OF 38 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-638013 [73] WPIDS
DOC. NO. CPI: C2001-188727
TITLE: Generating hemidesmosome-promoting laminin-5, comprises contacting the laminin-5 with plasmin under conditions for the plasmin to cleave the alpha3 subunits or contacting the cleaved alpha3 subunits with gamma2 and beta3 subunits.
DERWENT CLASS: B04 D16
INVENTOR(S): GOLDFINGER, L E; JONES, J C R; STACK, M S
PATENT ASSIGNEE(S): (NOUN) UNIV NORTHWESTERN
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6294356	B1	20010925	(200173)*		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6294356	B1 Provisional	US 1998-71663P	19980116
		US 1999-232394	19990115

PRIORITY APPLN. INFO: US 1998-71663P 19980116; US 1999-232394 19990115
AB US 6294356 B UPAB: 20011211
NOVELTY - Generating hemidesmosome-promoting laminin-5, comprising contacting the laminin-5 with plasmin under conditions effective so that the plasmin cleaves the alpha 3 subunits or contacting the cleaved alpha 3 subunits with gamma 2 and beta 3 subunits so that the 3 subunits combine to form the hemidesmosome-promoting laminin-5, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the

following:
(1) generating hemidesmosome-promoting laminin-5 comprising:
(a) culturing epithelial cells that do not produce hemidesmosome-promoting laminin-5 under conditions effective for the production of extracellular matrix protein comprising laminin-5 containing unprocessed alpha 3 subunits; and
(b) contacting the laminin-5 with plasmin under conditions effective so that the plasmin cleaves the alpha 3 subunits;
(2) generating hemidesmosome-promoting laminin-5 comprising:
(a) producing heterotrimeric laminin-5 containing unprocessed alpha 3 subunits by expressing DNA coding for alpha 3, gamma 2 and beta 3 subunits in host cells transformed with the DNA; and
(b) contacting the laminin-5 with plasmin under conditions for the plasmin to cleave the alpha 3 subunits; and
(3) generating hemidesmosome-promoting laminin-5 comprising:
(a) contacting a material containing unprocessed alpha 3 subunits of **laminin-5**, but not **gamma 2** or beta 3 subunits of **laminin-5**, with plasmin under conditions for the plasmin to cleave the alpha 3 subunits; and
(b) contacting the cleaved alpha 3 subunits with gamma 2 and beta 3 subunits so that the 3 subunits combine to form the hemidesmosome-promoting laminin-5.
USE - For making and using the 2 forms of laminin-5 and products comprising the 2 forms of laminin-5. Hemidesmosome-promoting laminin-5 can be used to stimulate hemidesmosome assembly by epithelial cells.
Dwg.0/0

L104 ANSWER 6 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001414630 EMBASE
TITLE: Expression of the invasion factor laminin .**gamma**. **2** in colorectal carcinomas is regulated by .beta.-catenin.
AUTHOR: Hlubek F.; Jung A.; Kotzor N.; Kirchner T.; Brabletz T.
CORPORATE SOURCE: T. Brabletz, Department of Pathology, University of Erlargen-Nurnberg, Krankenhausstr. 8-10, 91054 Erlangen, Germany. thomas.brabletz@patho.imed.uni-erlangen.de
SOURCE: Cancer Research, (15 Nov 2001) 61/22 (8089-8093).
Refs: 24
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The migration-inducing .**gamma**.**2** chain of laminin-5, one of the best known invasion markers, is strongly overexpressed in disseminating and infiltrating tumor cells at the invasive front of colorectal carcinomas. The same tumor cells show nuclear accumulation of the oncoprotein .beta.-catenin, which together with T-cell factor-DNA-binding proteins, functions as transcriptional activator of genes involved in tumor progression. Here we show that .beta.-catenin activates the human laminin-5 .**gamma**.**2** gene through two T-cell factor-binding elements in a synergistic manner together with hepatocyte growth factor and conclude that laminin-5 .**gamma**. **2** is another important target gene of nuclear .beta.-catenin during tumor progression.

L104 ANSWER 7 OF 38 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE

ACCESSION NUMBER: 2001:32783230 BIOTECHNO
TITLE: Cooperative interactions of **laminin 5 .gamma.2** chain, matrix metalloproteinase-2, and membrane type-1-matrix/metalloproteinase are required for mimicry of embryonic vasculogenesis by aggressive melanoma
AUTHOR: Seftor R.E.B.; Seftor E.A.; Koshikawa N.; Meltzer P.S.; Gardner L.M.G.; Bilban M.; Stetler-Stevenson W.G.; Quaranta V.; Hendrix M.J.C.
CORPORATE SOURCE: M.J.C. Hendrix, Department of Anatomy, University of Iowa, 1-100 BSB, 51 Newton Road, Iowa City, IA 52242-1109, United States.
E-mail: mary-hendrix@uiowa.edu
SOURCE: Cancer Research, (01 AUG 2001), 61/17 (6322-6327), 20 reference(s)
CODEN: CNREA8 ISSN: 0008-5472
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Vasculogenic mimicry describes a process where aggressive **tumor** cells in three-dimensional matrices mimic embryonic vasculogenesis by forming extracellular matrix (ECM)-rich, patterned tubular networks. Microarray gene chip analyses revealed significant increases in the expression of **laminin 5** (Ln-5, .**gamma**.
2 chain) and matrix metalloproteinases (MMP)-1, -2, -9, and MT1-MMP (MMP-14) in aggressive compared with poorly aggressive melanoma cells. These components colocalized with developing patterned networks and antisense oligonucleotides to the Ln-5 .gamma.2 chain (but not sense oligonucleotides), and **antibodies** to MMP-2 or MT1-MMP (but not MMP-9) inhibited the formation of these networks. Cultures which did not receive **antibodies** to either MMPs-2 or -14 contained the Ln-5 .gamma.2 chain promigratory cleavage fragments. Poorly aggressive melanoma cells seeded on collagen I matrices preconditioned by the aggressive cells formed tubular networks along the Ln-5 .gamma.2 chain-enriched tracks deposited by the aggressive cells. These results suggest that increased expression of MMP-2 and MT1-MMP, along with matrix deposition of the Ln-5 .gamma.2 chain and/or its cleavage fragments, are required for vasculogenic mimicry by aggressive melanoma cells. Furthermore, the apparent recapitulation of laminin-rich, patterned networks observed in aggressive melanoma patients' tissue sections by aggressive melanoma **tumor** cells in three-dimensional culture may also serve as a model to help identify specific molecular targets which could function as templates for the coordinated migration of aggressive **tumor** cells and their proteolytic remodeling of the ECM and may have profound implications for the development of novel therapies directed at the ECM to alter **tumor** progression.

L104 ANSWER 8 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001141353 EMBASE
TITLE: Increased expression of laminin-5 and its prognostic significance in lung adenocarcinomas of small size: An immunohistochemical analysis of 102 cases.
AUTHOR: Moriya Y.; Niki T.; Yamada T.; Matsuno Y.; Kondo H.; Hirohashi S.
CORPORATE SOURCE: Dr. S. Hirohashi, Pathology Division, Natl. Cancer Ctr. Research Institute, Chuo-ku, 104-0045 Tokyo, Japan
SOURCE: Cancer, (15 Mar 2001) 91/6 (1129-1141).
Refs: 47
ISSN: 0008-543X CODEN: CANCAR

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB BACKGROUND. Laminin-5 plays an important role in cell migration during tissue remodeling and tumor invasion. METHODS. The authors studied the expression of laminin-5 immunohistochemically in 102 cases of small-sized lung adenocarcinoma (maximum dimension .ltoreq. 2 cm) using a monoclonal antibody against the laminin .**gamma**.2 chain, and they also investigated the associations of laminin-5 with clinicopathologic characteristics. Prognostic significance of increased laminin-5 expression was evaluated using the Kaplan-Meier method and the Cox proportional hazard model. RESULTS. Overall, laminin-5 expression was observed in 82 cases (80.4%): 7 of 18 (38.9%) bronchioloalveolar carcinomas and 75 of 84 (89.3%) invasive adenocarcinomas. Laminin-5 was preferentially localized in the cytoplasm of tumor cells at the tumor-stromal interface, where budding or dissociation of cancer cells was frequently observed. Overexpression of laminin-5 (24 cases, 23.5%) was associated with vascular invasion (P = 0.021) and stromal fibroblastic reaction (P = 0.005) but not with nodal involvement, lymphatic invasion, or pleural invasion. Survival analysis revealed that overexpression of laminin-5 was associated with shorter patient survival (P = 0.0027 by log rank test). On multivariate analysis, overexpression of laminin-5 was an independent prognostic factor (P = 0.030), as were nodal involvement (P < 0.0001), vascular invasion (P = 0.047), and lymphatic invasion (P = 0.0047) in a whole cohort of patients. Moreover, when patients with Stage I (International Union Against Cancer [UICC] staging system) disease were considered in multivariate analysis, overexpression of laminin-5 was the only significant prognostic factor (P = 0.022), whereas vascular invasion had a marginally significant impact (P = 0.07) on patient survival. CONCLUSIONS. The authors' results showed that laminin-5 is frequently expressed by cancer cells at the invasive front of lung adenocarcinoma. The study concluded that overexpression of laminin-5 may be a useful prognostic factor in patients with small-sized lung adenocarcinoma, especially in Stage I cases. .COPYRGT. 2001 American Cancer Society.

L104 ANSWER 9 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001273091 EMBASE
TITLE: Expression of the .**gamma**.(2) chain of laminin-5 at the invasive front is associated with recurrence and poor prognosis in human esophageal squamous cell carcinoma.
AUTHOR: Yamamoto H.; Itoh F.; Iku S.; Hosokawa M.; Imai K.
CORPORATE SOURCE: H. Yamamoto, First Dept. of Internal Medicine, Sapporo Medical University, South-1, West-16, Chuo-ku, Sapporo 060-8543, Japan. h-yama@sapmed.ac.jp
SOURCE: Clinical Cancer Research, (2001) 7/4 (896-900).
Refs: 27
ISSN: 1078-0432 CODEN: CCREF4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose: Preferential expression of the .**gamma**.(2)

chain of laminin-5 in invading carcinoma cells has been implicated in tumor invasion. The aim of this study was to clarify the clinicopathological and prognostic significance of laminin .**gamma**.(2) chain expression in esophageal squamous cell carcinoma (SCC). Experimental Design: We analyzed the association between immunohistochemically detected laminin .**gamma**.(2) chain expression in esophageal SCC and clinicopathological characteristics, and we investigated whether laminin .**gamma**.(2) chain is a predictor of recurrence and/or survival. Results: The cytoplasm of carcinoma cells was stained for laminin .**gamma**.(2) at levels much stronger than those in normal esophageal basement membrane. The immunoreactivities at the invasive front were often more intense than those at the superficial layer. Sections with immunostaining signals in >30% of carcinoma cells at the invasive front, which were observed in 44 of 100 cases, were judged to be positive for laminin .**gamma**.(2) chain. Laminin .**gamma**.(2) chain positivity was significantly correlated with depth of invasion, lymph node metastasis, distant metastasis, advanced pTNM stage, recurrence, and recurrence within the first postoperative year. Patients with laminin .**gamma**.(2) chain-positive carcinoma had a significantly shorter disease-free and overall survival time than did those with laminin .**gamma**.(2) chain-negative carcinoma. Laminin .**gamma**.(2) chain retained its significant predictive value for disease-free and overall survival in multivariate analysis that included conventional clinicopathological factors. Conclusions: Our results suggest that the laminin .**gamma**.(2) chain plays a key role in the progression of esophageal carcinoma and that its detection is useful for the prediction of recurrence and poor prognosis.

L104 ANSWER 10 OF 38 CANCERLIT
ACCESSION NUMBER: 2001102157 CANCERLIT
DOCUMENT NUMBER: 21102157
TITLE: Keratinocyte migration requires alpha2beta1 integrin-mediated interaction with the **laminin 5 gamma2** chain.
AUTHOR: Decline F; Rousselle P
CORPORATE SOURCE: Institut de Biologie et Chimie des Proteines, UMR 5086, 7, passage du Vercors, 69367 Lyon cedex 07, France.
SOURCE: JOURNAL OF CELL SCIENCE, (2001). Vol. 114, Pt. 4, pp. 811-23.
Journal code: HNK. ISSN: 0021-9533.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; I
LANGUAGE: English
OTHER SOURCE: MEDLINE 21102157
ENTRY MONTH: 200104
AB Keratinocyte migration is an absolute requirement for correct epithelialization during the process of wound healing. This process requires changes in extracellular matrix ligand expression as well as changes in ligand-binding affinity of the corresponding cellular integrins. In this study, we attempt to understand the role of laminin 5 in migration by investigating the integrin-mediated interactions of migrating keratinocytes with their newly synthesized laminin 5. We chose to induce migration of freshly isolated NHK in vitro by exposing them to TGF-beta1 which, in addition to promoting epithelial cell migration, is also known to prevent cell proliferation. This important feature allowed the study to be focused on cell migration without interfering with cell proliferation. We confirm that keratinocyte migration on plastic, fibronectin or collagen IV substrates requires endogenous laminin 5

deposition, which is predominantly detected under its unprocessed form. Despite a crucial role for laminin 5 in migration, we show that this process is accompanied by a significant decrease in adhesion to purified laminin 5. Moreover, we provide evidence that the alpha2beta1 integrin interaction with newly synthesized laminin 5 renders the cells more adherent and retards migration. Conversely, we provide evidence that the alpha2beta1 integrin-laminin 5 interaction is absolutely required for keratinocyte migration and that the alpha2beta1 integrin is responsible for cell spreading on laminin 5. Finally, we demonstrate that the alpha2beta1 integrin binding to laminin 5 occurs within the short arm of the gamma2 subunit.

L104 ANSWER 11 OF 38 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 2001:32974479 BIOTECHNO
TITLE: Altered expression of collagen XVII in ameloblastomas and basal cell carcinomas
AUTHOR: Parikka M.; Kainulainen T.; Tasanen K.; Bruckner-Tuderman L.; Salo T.
CORPORATE SOURCE: T. Salo, Institute of Dentistry, University of Oulu, P.O. Box 5281, 90014 Oulu, Finland. E-mail: Tuula.Salo@oulu.fi
SOURCE: Journal of Oral Pathology and Medicine, (2001), 30/10 (589-595), 46 reference(s) CODEN: JPMEEA ISSN: 0904-2512
DOCUMENT TYPE: Journal; Article
COUNTRY: Denmark
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Collagen XVII (BP180) is an epithelial transmembrane protein, which presumably plays a role in cell migration and differentiation under both physiological and pathological conditions. Ameloblastoma, the most common odontogenic **neoplasm**, and basal cell carcinoma (BCC) of the skin exhibit similar growth patterns and share histological features. Methods: Here, we examined the distribution and expression of collagen XVII in ameloblastomas and BCCs using immunohistochemistry and non-radioactive in situ hybridization. In both **tumors**, the distribution of collagen XVII varied in different parts of the lesions. Results: In ameloblastomas, immunostaining for collagen XVII was usually localized in the basal and suprabasal cells of the **tumor** nests, although in some **tumors**, a diffuse intracellular staining was detected in the central cells of the neoplastic islands. In BCCs, collagen XVII was mostly seen as diffuse cytoplasmic staining in some central and peripheral cells of the **tumor** islands and also at the cell membranes in the basal keratinocytes of the epidermis overlying the **tumor** nests. Double immunostaining with **antibody** against .**gamma**.**2** chain of **laminin-5** showed that these two components of the keratinocyte adhesion complex are usually co-localized in ameloblastomas and BCCs. In both **tumors**, collagen XVII mRNA was found in the basal epithelial cells and in some central and peripheral cells of the **tumor** islands, while the stromal cells were negative. Conclusions: These findings indicate that the expression of collagen XVII may be differentially regulated in various parts of the **tumor**. Diffuse intracellular distribution of collagen XVII and a consequent loss of critical cellular attachments may contribute to the infiltrative and progressive growing potential of **tumors**.

L104 ANSWER 12 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001320383 EMBASE
TITLE: Biological and clinical relevance of Laminin-5 in cancer.

AUTHOR: Giannelli G.; Antonaci S.
CORPORATE SOURCE: G. Giannelli, Dipartimento di Clinica Medica, Clinica Medica II, Piazza G. Cesare 11, 70124 Bari, Italy. g.giannelli@intmed.uniba.it
SOURCE: Clinical and Experimental Metastasis, (2001) 18/6 (439-443).
Refs: 50
ISSN: 0262-0898 CODEN: CEXMD2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The occurrence of metastases is the hallmark of cancer. Development of metastasis severely affects prognosis and survival. It limits or discourages therapeutic interventions since no therapies are available to block or prevent cancer invasion. In order to invade, epithelial cancer cells need to penetrate through the basement membrane (BM) and remove extra-cellular matrix (ECM) tissue boundaries. In this context, proteases play a key role since they can either degrade or process the ECM components and thereby support cancer cell invasion. Laminin-5 (Ln-5) is an ECM protein, expressed predominantly in the BM structure, that promotes static adhesion and hemidesmosome formation. However, it also stimulates cell migration and/or invasion after having been cleaved by matrix metalloproteinases (MMPs) such as MMP-2 and MT1-MMP. Based on its dual functions, it would be intriguing to elucidate the role that Ln-5 plays in cancer cell motility and metastasis. One possibility is that MMPs, secreted by cancer cells or by neighbouring stromal cells, can cleave the .**gamma**.2 chain of Ln-5 deposited along the advancing edge of tumors. Ln-5, and in particular its .**gamma**.2 chain, has been found to be preferentially expressed in the cytoplasm of epithelial human cancer cells located at the advancing edge of the tumor. Such a distribution, which is restricted only to malignancies, suggests that the .**gamma**.2 chain may be implicated in epithelial cancer growth and invasion. Although the clinical significance of this finding is not yet clear, it seems often to be associated with a more aggressive and invasive cancer phenotype. This article will review the current body of evidence implicating the Ln-5 molecule, and in particular its .**gamma**.2 chain, as an important player in the tumor cascade and progression to metastatic disease. This will then be followed by a discussion of the presented data and its limitations. Finally, suggestions will be provided to improve the current state of knowledge in the field and future implications will be briefly discussed.

L104 ANSWER 13 OF 38 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-687538 [67] WPIDS
CROSS REFERENCE: 2000-687539 [67]
DOC. NO. NON-CPI: N2000-508294
DOC. NO. CPI: C2000-209323
TITLE: Laminin 5-expressing cells, used to accelerate wound healing associated with diabetic foot ulcers, venous ulcers, pressure sores, skin surgery, burns, acute wounds and skin grafts.
DERWENT CLASS: B04 D16 P34
INVENTOR(S): BOUTAUD, A
PATENT ASSIGNEE(S): (BIOS-N) BIOSTATUM INC
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2000066731 A2 20001109 (200067)* EN 230
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000046753 A 20001117 (200111)
EP 1177290 A2 20020206 (200218) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000066731	A2	WO 2000-US11459	20000428
AU 2000046753	A	AU 2000-46753	20000428
EP 1177290	A2	EP 2000-928524	20000428
		WO 2000-US11459	20000428

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000046753	A	Based on	WO 200066731
EP 1177290	A2	Based on	WO 200066731

PRIORITY APPLN. INFO: US 1999-155945P 19990924; US 1999-131720P 19990430; US 1999-149738P 19990821

AB WO 200066731 A UPAB: 20020319
NOVELTY - Recombinant laminin 5-expressing cells, are new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) purifying recombinant laminin 5, comprising growing the novel cells under expression conditions and passing the cell culture medium through an affinity chromatography column which contains a compound binding specifically to the epitope tag, washing the column to remove unbound material, and eluting the bound recombinant laminin 5;
(2) purified recombinant laminin 5 (I), optionally isolated by the method of (1);
(3) a pharmaceutical composition (II) comprising (I), and a carrier;
(4) an improved cell growth substrate which has been coated with (I) or (II) to promote cell attachment to the substrate;
(5) an improved cell culture medium including (I) which promotes attachment to a cell growth substrate;
(6) an improved medical implant device coated with (I) or (II) to promote cell attachment to the device;
(7) improving the biocompatibility of a medical device, comprising contacting the cells with (II);
(8) an isolated polynucleotide comprising a 3585, 3469, 3720, or 3620 nucleotide sequence, all fully defined in the specification; and
(9) an isolated polypeptide comprising a 1174, 1155, 1193, or 1172 residue amino acid sequence, all fully defined in the specification.
ACTIVITY - Vulnerary; antiulcer; antiinflammatory; antidiabetic. No biological data is given.
MECHANISM OF ACTION - Cell adhesion promoter.
USE - (I) and (II) are used to accelerate wound healing, especially

diabetic foot ulcers, venous ulcers, pressure sores, skin surgery, burns, acute wounds, skin grafts, corneal ulcerations, gastro-intestinal ulcers, periodontitis, and gingivitis. They are also used to improve the biocompatibility of medical devices, and to promote cell adhesion to a surface. The medical device is an implantation device selected from artificial grafts, indwelling or transcutaneous catheter, polytetrafluoroethylene, expanded polytetrafluoroethylene, needle, metal pin, metal rod, colostomy tube, dental abutment piece or surgical mesh. They can be used for the ex vivo treatment of Type I diabetes, by culturing isolated pancreatic islet beta cells in the presence of (I) or (II), and then re-introducing the cells into the patient. (All claimed). Laminin can also be used to regulate angiogenesis.

ADVANTAGE - The cell line produces and secretes recombinant heterotrimeric laminin, prior art cell lines have produced cells producing but not secreting only one or two chain laminins.

Dwg.0/3

L104 ANSWER 14 OF 38 CANCERLIT
ACCESSION NUMBER: 2000526085 CANCERLIT
DOCUMENT NUMBER: 20526085
TITLE: Tumor cell budding and laminin-5 expression in colorectal carcinoma can be modulated by the tissue micro-environment.
AUTHOR: Sordat I; Rousselle P; Chaubert P; Petermann O; Aberdam D; Bosman F T; Sordat B
CORPORATE SOURCE: Unit of Experimental Pathology, Swiss Institute for Experimental Cancer Research, Epalinges, Lausanne, Switzerland.
SOURCE: INTERNATIONAL JOURNAL OF CANCER, (2000). Vol. 88, No. 5, pp. 708-17.
Journal code: GQU. ISSN: 0020-7136.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; I
LANGUAGE: English
OTHER SOURCE: MEDLINE 20526085
ENTRY MONTH: 200101

AB Expression of laminin-5 alpha3, beta3 and gamma2 protein subunits was investigated in colorectal adenocarcinomas using immunostaining and confocal microscopy. The laminin-5 heterotrimer was found in basement membranes and as extracellular deposits in tumor stroma. In contrast to the alpha3 subunit, which was under-expressed, the gamma2 and beta3 subunits were detected in the cytoplasm of carcinoma cells dissociating (budding) from neoplastic tubules, suggestive of focal alterations in laminin-5 assembly and secretion. **Laminin-5 gamma2** or beta3 subunit-reactive budding carcinoma cells expressed cytokeratins but not vimentin; they did not proliferate and were not apoptotic. Furthermore, expression of **laminin-5 gamma2** and beta3 subunits in budding cells was associated with focal under-expression of the E-cadherin-beta-catenin complex. Results from xenograft experiments showed that budding activity in colorectal adenocarcinomas could be suppressed when these tumors grew at ectopic s.c. sites in nude mice. In vitro, cultured colon carcinoma cells, but not adenoma-derived tumor cells, shared the laminin-5 phenotype expressed by carcinoma cells in vivo. Using colon carcinoma cell lines implanted orthotopically and invading the cecum of nude mice, the laminin-5-associated budding was restored, indicating that this phenotype is not only determined by tumor cell properties but also dependent on the tissue micro-environment. Our results indicate that both laminin-5 alpha3 subunit expression and cell-cell cohesiveness are altered in budding carcinoma cells, which we consider to be actively invading. We propose that the local tissue micro-environment contributes to these events.

L104 ANSWER 15 OF 38 CANCERLIT
ACCESSION NUMBER: 2000422278 CANCERLIT
DOCUMENT NUMBER: 20422278
TITLE: Differential expression of the LAMB3 and LAMC2 genes between small cell and non-small cell lung carcinomas.
AUTHOR: Manda R; Kohno T; Niki T; Yamada T; Takenoshita S; Kuwano H; Yokota J
CORPORATE SOURCE: Biology, Pathology Divisions, National Cancer Center Research Institute, 1-1, Tsukiji 5-chome, Tokyo, Chuo-ku, 104-0045, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2000). Vol. 275, No. 2, pp. 440-5.
Journal code: 9Y8. ISSN: 0006-291X.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 20422278
ENTRY MONTH: 200011
AB To identify genes differentially expressed between small cell lung carcinoma (SCLC) cells and non-SCLC cells, mRNA differential display was applied to 3 SCLC cell lines and 6 non-SCLC cell lines. The LAMB3 gene was identified as being expressed only in non-SCLC cells and not in SCLC cells. The LAMB3 gene encodes the laminin beta3 chain, which is a unique component of laminin-5. Laminin-5 is a heterotrimer protein consisting of the alpha3, beta3, and gamma2 chains, and another unique component of **laminin-5** is the **gamma2** chain encoded by the LAMC2 gene. RT-PCR analysis of the LAMB3 and LAMC2 genes in 45 lung cancer cell lines revealed that both the LAMB3 and LAMC2 genes were co-expressed in 21 of 32 non-SCLC cell lines (66%) but only in one of 13 SCLC cell lines (8%). Coexpression of the LAMB3 and LAMC2 genes was also observed in all 4 cases of primary non-SCLC cells examined but not in the corresponding non-cancerous lung cells. Since alpha6beta4 integrin, the specific laminin-5 binding receptor, is known to be expressed only in non-SCLC cells and not in SCLC cells, it was indicated that laminin-5 is a critical microenvironmental factor for the growth of non-SCLC cells but not of SCLC cells. The differences in the expression of integrins and laminins would be critical factors to distinguish SCLC and non-SCLC cells, and such differences might be associated with the unique biological properties of SCLC cells, including metastatic potential and drug sensitivity. Copyright 2000 Academic Press.

L104 ANSWER 16 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000415250 EMBASE
TITLE: Cancer of the vagina: Laminin-5.**gamma**.2 chain expression and prognosis.
AUTHOR: Hellman K.; Hellstrom A.-C.; Silfversward C.; Salo S.; Aspenblad U.; Nilsson B.; Frankendal B.; Tryggvasson K.; Auer G.
CORPORATE SOURCE: Dr. K. Hellman, Department of Gynecological Oncology, Radiumhemmet, Karolinska Hospital, S-17176 Stockholm, Sweden. Kristina.Hellman@onkpat.ki.se
SOURCE: International Journal of Gynecological Cancer, (2000) 10/5 (391-396).
Refs: 37
ISSN: 1048-891X CODEN: IJGCEN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology

016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The purpose of this experiment was to investigate the expression and the prognostic impact of the .**gamma**.2 subchain of laminin-5 in vaginal malignancies. The outcome of the rare disease primary carcinoma of the vagina is poor and little is known about prognostic markers. The .**gamma**.2 chain of laminin-5, an epithelial basement membrane protein, is thought to play a crucial role in tumor cell adhesion, migration, and proliferation, and may thus be an additive potential marker. Archival, paraffin-embedded sections were stained immunohistochemically with an antibody against the .**gamma**.2 chain of human laminin-5 protein. The material consisted of 59 cases of primary vaginal malignancies, subdivided into short- and long-time survivors. All invasive malignancies of epithelial origin were positively stained with the antibody against the .**gamma**.2 chain. High expression of the .**gamma**.2 chain correlated significantly in an univariate analysis with short-time survival (P = 0.041), but in the multivariate analysis only age and tumor size were independent prognostic factors. A significant intercorrelation between large tumors and high .**gamma**.2 chain immunoreactivity was found (P = 0.003). These results indicate that laminin-5.**gamma**.2 subchain expression in primary vaginal carcinomas is of prognostic impact. However, in a multivariate analysis only patient age and tumor size had independent prognostic value.

L104 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:795994 HCAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
GB 1998-12099	A	19980606
GB 1998-13291	A	19980620
GB 1998-13611	A	19980624
GB 1998-13835	A	19980627
GB 1998-14110	A	19980701
GB 1998-14580	A	19980707
GB 1998-15438	A	19980716

GB 1998-15574	A	19980718
GB 1998-15576	A	19980718
GB 1998-16085	A	19980724
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L104 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:795993 HCAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,

MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
GB 2339200	B2	20010912		
EP 1084273	A1	20010321	EP 1999-925207	19990604

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.:

GB 1998-12098	A	19980606
GB 1998-28289	A	19981223
GB 1998-16086	A	19980724
GB 1998-16921	A	19980805
GB 1998-17097	A	19980807
GB 1998-17200	A	19980808
GB 1998-17632	A	19980814
GB 1998-17943	A	19980819
WO 1999-GB1779	W	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L104 ANSWER 19 OF 38 CANCERLIT

ACCESSION NUMBER: 2000019468 CANCERLIT
DOCUMENT NUMBER: 20019468
TITLE: Overexpression of laminin **gamma2** chain monomer in invading gastric carcinoma cells.
AUTHOR: Koshikawa N; Moriyama K; Takamura H; Mizushima H; Nagashima Y; Yanoma S; Miyazaki K
CORPORATE SOURCE: Division of Cell Biology, Kihara Institute for Biological Research, Yokohama City University, Japan.
SOURCE: CANCER RESEARCH, (1999). Vol. 59, No. 21, pp. 5596-601. Journal code: CNF. ISSN: 0008-5472.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 20019468
ENTRY MONTH: 200001
AB Laminin (LN)-5, a heterotrimer of alpha3, beta3, and **gamma2** chains, has been suggested to be involved in tumor cell invasion. The present immunohistochemical study investigated the distribution of the LN **gamma2** chain in 48 different human gastric adenocarcinomas. The immunohistochemical analysis showed two distinct patterns of LN **gamma2** chain expression: (a) extracellular deposition; and (b)

cytoplasmic accumulation. The extracellular deposition of the LN **gamma2** chain was typically observed at neoplastic basement membranes of well-differentiated adenocarcinomas. The immunoreactivity was continuous along tumor basement membranes in these tumors but was irregular and diffuse in poorly differentiated carcinomas. These tumor cells coexpressed the LN alpha3 and beta3 chains, suggesting that the LN **gamma2** chain was deposited as the LN-5 complex. In contrast, tumor cells at the invading fronts showed strong cytoplasmic staining for the LN **gamma2** chain without any detectable signal for the LN alpha3 or beta3 chain in both well- and poorly differentiated carcinomas. On the other hand, in vitro analysis by two-dimensional SDS-PAGE demonstrated that human gastric carcinoma cells secrete a high level of LN **gamma2** chain monomer in addition to the LN-5 complex into culture medium. These results indicate that the LN **gamma2** chain can be secreted as a single subunit and might be involved in tumor cell invasion.

L104 ANSWER 20 OF 38 CANCERLIT DUPLICATE 2
ACCESSION NUMBER: 1999323918 CANCERLIT
DOCUMENT NUMBER: 99323918
TITLE: The SFL activity secreted by metastatic carcinoma cells is related to **laminin 5** and mediates cell scattering in an integrin-independent manner.
AUTHOR: Grassi M; Moens G; Rousselle P; Thiery J P; Jouanneau J
CORPORATE SOURCE: Laboratoire de Morphogenese cellulaire et Progression tumorale, CNRS/Institut Curie, UMR 144, 75248 Paris Cedex 05, France.
SOURCE: JOURNAL OF CELL SCIENCE, (1999). Vol. 112, Pt. 15, pp. 2511-20.
Journal code: HNK. ISSN: 0021-9533.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 99323918
ENTRY MONTH: 199911
AB We have previously reported that an in vivo-selected metastatic variant of NBT-II rat carcinoma cells, M-NBT-II, produces and secretes a factor with cell-scattering activity, SFL, that is potentially involved in tumor progression. This biological activity was purified and characterized as a **laminin 5** (LN5) -related protein. This SFL/LN5 protein consists of the (alpha)3, (beta)3 and (gamma)2 chains of expected sizes. **Laminin 5** is a multifunctional secreted glycoprotein thought to be involved in cell adhesion and migration, mainly via its interaction with (alpha)3(beta)1 and (alpha)6(beta)4 integrins. SFL/LN5, and purified human **laminin 5**, induced the scattering and motility of MDCK cells and the formation of actin stress fibers and focal contacts in A549 cells. These events were dependent on activation of the small GTP-binding protein Rho. (Alpha)v colocalized with vinculin in the focal contacts of activated cells whereas (alpha)3 and (alpha)6 integrins did not. Blocking antibodies directed against (alpha)3 and (alpha)6 integrins or the **laminin 5** integrin-binding site did not abolish SFL/LN5 biological activity, which, in contrast, was completely inhibited by heparin. Thus, SFL/LN5 activity in epithelial cell scattering and cytoskeletal reorganization is probably independent of integrin receptors.

L104 ANSWER 21 OF 38 CANCERLIT
ACCESSION NUMBER: 1999284291 CANCERLIT
DOCUMENT NUMBER: 99284291
TITLE: Clinocopathologic significance of **laminin-5 gamma2** chain expression in squamous

cell carcinoma of the tongue: immunohistochemical analysis of 67 lesions.
AUTHOR: Ono Y; Nakanishi Y; Ino Y; Niki T; Yamada T; Yoshimura K; Saikawa M; Nakajima T; Hirohashi S
CORPORATE SOURCE: Pathology Division, National Cancer Center Research Institute, Tokyo, Japan.
SOURCE: CANCER, (1999). Vol. 85, No. 11, pp. 2315-21.
Journal code: CLZ. ISSN: 0008-543X.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Abridged Index Medicus Journals; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 99284291
ENTRY MONTH: 199907
AB BACKGROUND: The **laminin-5 gamma2** chain plays an important role in cell migration during tumor invasion and tissue remodeling. METHODS: **Laminin-5 gamma2** chain expression in squamous cell carcinomas of the tongue in 67 patients with Stage II, III, or IVA,B (excluding the cases with distant metastasis) was examined immunohistochemically to determine its associations with the clinicopathologic features of each tumor. The predominant staining patterns were categorized as follows: A, few or no tumor cells were positive; B, part of the tumor nest periphery was positive; C, the tumor nest periphery was circumferentially positive; or D, almost all the tumor cells were positive. RESULTS: **Laminin-5 gamma2** chain expression was observed clearly in tumor cell cytoplasm. Of the 67 tumors examined, 6 (9%), 31 (46%), 19 (28%), and 11 (17%) showed staining patterns A, B, C, and D, respectively. With progression from staining pattern A to D, the number of immunopositive tumor cells increased significantly ($P<0.0001$), and the tumor histology showed significantly more infiltrative growth ($P<0.0001$) and poorer differentiation ($P = 0.0021$). Furthermore, both univariate ($P = 0.0019$) and multivariate ($P = 0.0003$; hazard ratio = 3.132) analysis of the patients' survival revealed that the prognosis became significantly poorer with progression from staining pattern A to D. CONCLUSIONS: Increased **laminin-5 gamma2** chain immunoreactivity, which may reflect a high invasive potential of cancer cells, is a factor indicative of a poor prognosis for patients with squamous cell carcinoma of the tongue.

L104 ANSWER 22 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999414653 EMBASE
TITLE: Laminin-5 as a marker of invasiveness in cervical lesions.
AUTHOR: Skyldberg B.; Salo S.; Eriksson E.; Aspenblad U.; Moberger B.; Tryggvason K.; Auer G.
CORPORATE SOURCE: Dr. B. Skyldberg, Cancer Center Karolinska, Karolinska Hospital, S-171 76 Stockholm, Sweden. Barbro.Skyldberg@cck.ki.se
SOURCE: Journal of the National Cancer Institute, (3 Nov 1999) 91/21 (1882-1887).
Refs: 40
ISSN: 0027-8874 CODEN: JNCIAM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Background: Treatment decisions for cervical cancer, a common disease worldwide, depend on demonstrating whether or not tumor invasion of the

surrounding tissue has occurred. Invasion can be difficult to assess by standard histopathologic methods, especially when limited amounts of tissue are available. Several studies of a variety of cancers have reported increased expression of laminin-5-an important attachment protein for epithelial cells - in invasive carcinomas. This study was designed to investigate whether the presence of laminin-5 is related to the invasive capacity of cervical lesions. Methods: We used immunohistochemical methods to stain archival, paraffin-embedded sections of cervical lesions with a polyclonal antibody specifically targeting the .**gamma**.**2** chain of human laminin-5 protein. The study sample included 23 lesions of mild and moderate dysplasia (cervical intraepithelial neoplasia [CIN] 1 and 2, respectively), 32 lesions of severe dysplasia or carcinoma in situ (CIN 3), 15 lesions of microinvasive cancer, and 20 lesions of frankly invasive cancer. Cellular proliferative activity was also investigated by the use of monoclonal MIB-1 (directed against the antigen Ki-67) and anticyclin A antibodies. Results: Invasiveness of cervical lesions was positively associated with immunohistochemical staining of the .**gamma**.**2** chain of laminin-5 (two-sided P = .001). All CIN 1 and CIN 2 lesions - except one CIN 2 lesion later shown to be invasive cancer - and 21 CIN 3 lesions tested negative for the .**gamma**.**2** chain of laminin-5. Eleven CIN 3 lesions and all invasive cancers tested positive for this protein. One lymph node metastasis and a pleural metastasis from one of the patients with invasive cancer showed strong immunohistochemical positivity. Proliferative activity increased with advancement of the lesion but was not confined to cells positive for the .**gamma**.**2** chain of laminin-5. Conclusions: These data suggest that antibodies directed against the .**gamma**.**2** chain of laminin-5 can identify cervical lesions with invasive capacity and thus may be useful as a sensitive marker of early invasion.

L104 ANSWER 23 OF 38 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1999:29516154 BIOTECHNO
TITLE: Distribution of laminin and fibronectin isoforms in oral mucosa and oral squamous cell carcinoma
AUTHOR: Kosmehi H.; Berndt A.; Strassburger S.; Borsi L.; Rousselle P.; Mandel U.; Hyckel P.; Zardi L.; Katenkamp D.
CORPORATE SOURCE: H. Kosmehi, Institute of Pathology, Friedrich Schiller University, D-07740 Jena, Germany.
SOURCE: British Journal of Cancer, (1999), 81/6 (1071-1079), 66 reference(s)
CODEN: BJCAAI ISSN: 0007-0920
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The expression of laminin and fibronectin isoforms varies with cellular maturation and differentiation and these differences may well influence cellular processes such as adhesion and motility. The basement membrane (BM) of fetal oral squamous epithelium contains the laminin chains, .alpha.2, .alpha.3, .alpha.5, .beta.1, .beta.2, .beta.3, .gamma.1 and .gamma.2. The BM of adult normal oral squamous epithelium comprises the laminin chains, .alpha.3, .alpha.5, .beta.1, .beta.3, .gamma.1 and .**gamma**.**2**. A re-expression of the **laminin** .alpha.2 and .beta.2 chains could be shown in adult hyperproliferative, dysplastic and carcinomatous lesions. In dysplasia and oral squamous cell carcinoma (OSCC), multifocal breaks of the BM are present as indicated by laminin chain **antibodies**. These breaks correlate to malignancy grade in their extent. Moreover, in the **invasion** front the .alpha.3 and .**gamma**.**2** chain of **laminin**-

5 can immunohistochemically be found outside the BM within the cytoplasm of budding carcinoma cells and in the adjacent stroma. The correlation between the morphological pattern or **invasive** tumour clusters and a laminin-5 immunostaining in the adjacent stroma may suggest, first, that a laminin-5 deposition outside the BM is an immunohistochemical marker for **invasion** and second, that OSCC **invasion** is guided by the laminin-5 matrix. Expression of oncofetal fibronectins (IIICS de novo glycosylated fibronectin and ED-B fibronectin) could be demonstrated throughout the stromal compartment. However, the ED-B fibronectin synthesizing cells (RNA/RNA in situ hybridization) are confined to small stroma areas and to single stroma and inflammatory cells in the **invasion** front. A correlation of the number of ED-B fibronectin synthesizing cells to malignancy grade could not be seen. ED-B fibronectin mRNA-positive cells seem to be concentrated in areas of fibrous stroma recruitment with a linear alignment of stomal fibro-/myofibroblasts (desmoplasia). Double staining experiments (ED-B fibronectin in situ hybridization and .alpha.-smooth muscle actin immunohistochemistry) indicated that the stroma myofibroblasts are a preferential source of ED-B fibronectin. In conclusion, in OSCC, a fetal extracellular matrix conversion is demonstrable. Tumour cells (laminin .alpha.2 and .beta.2 chain) and recruited stromal myofibroblasts (oncofetal ED-B fibronectin) contribute to the fetal extracellular matrix milieu.

L104 ANSWER 24 OF 38 CANCERLIT
ACCESSION NUMBER: 1999406071 CANCERLIT
DOCUMENT NUMBER: 99406071
TITLE: Expression of laminin-5 in ameloblastomas and human fetal teeth.
AUTHOR: Salo T; Kainulainen T; Parikka M; Heikinheimo K
CORPORATE SOURCE: Department of Diagnostic and Oral Medicine, Institute of Dentistry, University of Oulu, Finland.
SOURCE: JOURNAL OF ORAL PATHOLOGY AND MEDICINE, (1999). Vol. 28, No. 8, pp. 337-42.
Journal code: JRF. ISSN: 0904-2512.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Dental Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 99406071
ENTRY MONTH: 199911

AB Extracellular matrix proteins have been shown to play important roles in the cell migration and differentiation in both normal and pathological conditions. In the present study, we used immunohistochemistry and in situ hybridization to determine the distribution of laminin-5 in ameloblastomas and developing human teeth. In ameloblastomas, the immunoreaction for the **laminin-5 gamma2** chain was confined to the tumor cells of the peripheral area. The staining reaction was variable, being mostly weak and fragmented in the basement membrane structures surrounding the neoplastic islands. Some peripheral epithelial cells and some invading small ameloblastoma cell islands showed intense intracellular staining for the gamma2 chain. Tumor cells in the proliferating areas of ameloblastomas expressed gamma2 chain mRNA. The **laminin-5 gamma2** chain was located beneath the dental lamina and in the outer, but not in the inner, enamel epithelium of the developing teeth. During the early hard tissue apposition stage, intense staining for the gamma2 chain was confined to ameloblasts, which also gave a strong signal for gamma2 chain mRNA. These results suggest that laminin-5 may contribute to the infiltrative and progressive growing potential of ameloblastomas. During human tooth development, however, laminin-5 may participate in the terminal differentiation of ameloblasts

and in enamel matrix formation.

L104 ANSWER 25 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999174062 EMBASE
TITLE: Loss of laminin-5 in the epithelium-stroma interface: An immunohistochemical marker of malignancy in epithelial lesions of the breast.
AUTHOR: Henning K.; Berndt A.; Katenkamp D.; Kosmehl H.
CORPORATE SOURCE: Prof. H. Kosmehl, Institute of Pathology, Friedrich Schiller University, D-07740 Jena, Germany. kosmehl@bach.med.uni-jena.de
SOURCE: Histopathology, (1999) 34/4 (305-309).
Refs: 27
ISSN: 0309-0167 CODEN: HISTDD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Aims: To demonstrate immunohistochemically the .alpha.3 and .**gamma**.**2** chain of laminin-5 in benign epithelial and malignant lesions of the human breast. Methods and results: The .alpha.3 chain was identified by the monoclonal antibody BM165 and the .**gamma**.**2** chain by GB3 in shock frozen samples using APAAP (alkaline phosphatase monoclonal anti-alkaline phosphatase) technique. The pre-existing breast epithelium, the 12 benign ductal and lobular proliferations and the three fibroadenomas showed a continuous immunostaining in the basement membrane region. In contrast to benign epithelial lesions, the 44 cases of invasive breast carcinoma showed a loss of the laminin-5 chains in more than 50% of the carcinoma stroma interface. Twenty-four out of the 44 invasive carcinomas revealed a complete loss of laminin-5 immunostaining. Focal defects of the laminin-5 immunostaining were also found in ductal carcinoma in situ in its pure form. Conclusions: As recently described, the malignant transformation of breast epithelium with expression of an invasive phenotype is associated with a decrease of hemidesmosomes. The reduced immunostaining of laminin-5 is in line with this finding because laminin-5 represents the major component of the anchoring filaments attaching hemidesmosomes to the basement membrane. We feel that immunohistochemical demonstration of laminin- 5 may serve as a marker of benignity in epithelial breast lesions. While other carcinoma types exhibit an increased laminin-5 deposition, which has been suggested as an invasion promoting factor, the loss of laminin-5 in breast cancer supports the view that breast carcinomas do not utilize laminin-5 for invasion.

L104 ANSWER 26 OF 38 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999173783 EMBASE
TITLE: Laminin-5 promotes adhesion and migration of epithelial cells: Identification of a migration-related element in the .**gamma**.**2** chain gene (LAMC2) with activity in transgenic mice.
AUTHOR: Salo S.; Haakana H.; Kontusaari S.; Hujanen E.; Kallunki T.; Tryggvason K.
CORPORATE SOURCE: K. Tryggvason, Biocenter Oulu, Department of Biochemistry, University of Oulu, FIN-90570 Oulu, Finland
SOURCE: Matrix Biology, (1999) 18/2 (197-210).
Refs: 55
ISSN: 0945-053X CODEN: MTBOEC
PUBLISHER IDENT.: S 0945-053X(99)00012-8
COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The effects of laminin-5 and its subunit .**gamma**.**2** chain on cell adhesion and migration were studied, and a migration-related cis-acting element was identified in the .**gamma**.**2** chain gene (LAMC2) using promoter-reporter gene constructs in transgenic mice. Intact laminin-5 molecules, but not recombinant .**gamma**.**2** chain promoted cell adhesion of human keratinocytes and mouse squamous carcinoma cells, indicating that the .**gamma**.**2** chain does not contain a cellular binding site. However, the .**gamma**.**2** chain as such is probably involved in the process of cell locomotion, as antibodies against the short arm of the chain inhibited migration of carcinoma cells in an in vitro assay. Further evidence for the involvement of the .**gamma**.**2** chain in cell migration was obtained by the identification of a cis-acting element in a promoter-lacZ reporter gene construct that was active in migratory epithelial cells of healing wounds in mice made transgenic by microinjection of the construct into fertilized oozytes. The migration active element was located in the sequence between -613 and +55. The same construct, and another one containing 5900 base pairs of the 5' flanking region, yielded very limited expression in cells of normal tissues. The limited expression was, however, only observed in epithelial cells of different tissues, i.e. cell types that normally express laminin-5 in vivo. The results show that the sequence between -613 and +55 contains elements that can drive expression during epithelial cell migration and that also partially confers more general epithelium expression. However, elements outside -5900 and +55 are needed for normal epithelium expression of the LAMC2 gene.

L104 ANSWER 27 OF 38 CANCERLIT
ACCESSION NUMBER: 1998311660 CANCERLIT
DOCUMENT NUMBER: 98311660
TITLE: Human colonic cancer cells synthesize and adhere to **laminin-5**. Their adhesion to **laminin-5** involves multiple receptors among which is integrin alpha2beta1.
AUTHOR: Orian-Rousseau V; Aberdam D; Rousselle P; Messent A; Gavrilovic J; Meneguzzi G; Kedinger M; Simon-Assmann P
CORPORATE SOURCE: INSERM U.381, 67200 Strasbourg, France.
SOURCE: JOURNAL OF CELL SCIENCE, (1998). Vol. 111, Pt. 14, pp. 1993-2004.
Journal code: HNK. ISSN: 0021-9533.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 98311660
ENTRY MONTH: 199810
AB In the mature gut, **laminin-5** is expressed at the basal aspect of the differentiating epithelial cells. In vitro, we show that three more or less differentiated human colonic cancer HT29 cell lines produce and deposit **laminin-5**; they predominantly synthesize and secrete the 440 kDa form of **laminin-5** that comprises the unprocessed 155 kDa **gamma2** chain, as determined by immunoprecipitation analysis. In contrast, the highly differentiated colon carcinoma Caco-2 cells produce almost no **laminin-5**. Using anti-integrin antibodies, we show that adhesion of the two colonic cancer cell lines to **laminin-5** is mediated by multiple integrin receptors including those for

alpha3beta1, alpha6beta1 and alpha6beta4 integrins like in other cell types. In addition, the implication of integrin alpha2beta1 in this adhesion process is demonstrated for the first time. This has been shown by cell adhesion inhibition experiments, solid phase assays and confocal analysis. Together with previous in situ observations, these data provide a baseline knowledge for the understanding of the regulation of **laminin-5** in normal and pathological intestine.

L104 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:805381 HCAPLUS
DOCUMENT NUMBER: 130:221969
TITLE: Antiepiligrin cicatricial pemphigoid represents an autoimmune response to subunits present in laminin 5 (.alpha.3.beta.3.gamma.2)
AUTHOR(S): Lazarova, Z.; Hsu, R.; Yee, C.; Yancey, K. B.
CORPORATE SOURCE: Dermatology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892-1908, USA
SOURCE: British Journal of Dermatology (1998), 139(5), 791-797
CODEN: BJDEAZ; ISSN: 0007-0963
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sera from 20 patients with antiepiligrin cicatricial pemphigoid were studied to define the specific reactivity of their IgG autoantibodies. IgG from all patients bound exclusively to the dermal side of 1 mol/L NaCl split skin and immunopptd. laminin 5 (.alpha.3.beta.3.gamma.2) from exts. of human keratinocytes (HKs). Immunoblot studies on purified laminin 5 subunits demonstrated that patient IgG bound .alpha.3 alone in 16 patients. In two patients, IgG autoantibodies were directed predominantly to the .gamma.2 subunit, yet showed trace reactivity to .alpha.3 as well. Sera from two patients did not immunoblot any laminin 5 subunits, their IgG presumably immunopptg. laminin 5 via a conformational epitope. Sera from patients with .alpha.3 subunit-specific IgG immunopptd. all subunits of laminin 5 as well as polypeptides of 190 and 200 kDa from the conditioned media of HKs. Preclearance studies and expts. utilizing affinity-purified patient IgG demonstrated that the latter signified laminin 6 (.alpha.3.beta.1.gamma.1) that was bound by cross-reactive .alpha.3 subunit-specific patient IgG. Sera from patients with .gamma.2 subunit-specific IgG showed no reactivity to laminin 6, except for faint reactivity provided by low levels of their .alpha.3 subunit-specific IgG. Taken together, these findings indicate that antiepiligrin cicatricial pemphigoid signifies an autoimmune response to subunits present in laminin 5.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L104 ANSWER 29 OF 38 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.DUPLICATE
ACCESSION NUMBER: 1998:28164570 BIOTECHNO
TITLE: Integrin .alpha.3.beta.1-mediated interaction with laminin-5 stimulates adhesion, migration and **invasion** of malignant glioma cells
AUTHOR: Fukushima Y.; Ohnishi T.; Arita N.; Hayakawa T.; Sekiguchi K.
CORPORATE SOURCE: K. Sekiguchi, Research Institute, Osaka Med. Ctr. Maternal/Child Hlth., 840 Murodo, Izumi, Osaka 590-02, Japan.
E-mail: j61639@center.osaka-u.ac.jp
SOURCE: International Journal of Cancer, (1998), 76/1 (63-72), 27 reference(s)

CODEN: IJCNAW ISSN: 0020-7136
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Gliomas, characterized by their progressively **invasive** phenotype, express integrin .alpha.3.beta.1 as a major receptor for the extracellular matrix both in vivo and in vitro. Since the integrin .alpha.3.beta.1 has been shown to be a specific receptor for **laminin-5** (.alpha.3.beta.3.**gamma.2**), we examined the effects of purified human laminin-5 on adhesion, migration and **invasion** of human glioma cells. Among different types of laminin variants and other matrix proteins including fibronectin and vitronectin, laminin-5 was most potent in promoting adhesion and migration of different kinds of glioma cells. Laminin-5-mediated adhesion and migration were specifically inhibited by monoclonal **antibodies** against integrin .alpha.3 and .beta.1 chains, confirming the role of integrin .alpha.3.beta.1 as the major laminin-5 receptor. **Invasion** of the reconstituted basement membrane (i.e., Matrigel) by glioma cells was also selectively stimulated by laminin-5. Out results show that laminin-5 is the major extracellular stimulant for glioma cell adhesion, migration and **invasion**. The immunohistochemical distribution of **laminin** .**gamma**. **2** chain, a **laminin** subunit unique to laminin-5, showed that it was expressed in the **tumor** parenchyma of human glioma tissues. Expression of **laminin** .alpha.3, .beta.3 and . **gamma.2** chains in glioma tissues and in glioma cell lines was also demonstrated at the messenger RNA level by reverse transcription polymerase chain reaction. Our results, taken together, show that laminin-5 may be involved in the **invasive** phenotype of malignant gliomas both in vitro and in vivo.

L104 ANSWER 30 OF 38 CANCERLIT DUPLICATE 4
ACCESSION NUMBER: 1998378981 CANCERLIT
DOCUMENT NUMBER: 98378981
TITLE: Differential expression of laminin-5 subunits and integrin receptors in human colorectal neoplasia.
AUTHOR: Sordat I; Bosman F T; Dorta G; Rousselle P; Aberdam D; Blum A L; Sordat B
CORPORATE SOURCE: Swiss Institute for Experimental Cancer Research (ISREC), Epalinges, Switzerland. bernard.sordat@isrec.unil.ch
SOURCE: JOURNAL OF PATHOLOGY, (1998). Vol. 185, No. 1, pp. 44-52. Journal code: JLB. ISSN: 0022-3417.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 98378981
ENTRY MONTH: 199810
AB Cell-matrix interactions contribute to regulating the adhesion, growth, migration, and differentiation of epithelial intestinal cells. Alterations in matrix components and their cellular receptors have been found in tumours but their specific roles remain unclear. The tissue patterns of laminin-5 and alpha 3, beta 3 and gamma 2 subunits, as well as those of the alpha 3, alpha 6, beta 1, and beta 4 integrin chains, were determined by immunofluorescence on frozen sections of 12 colorectal mucosal samples from four patients, 15 adenomas, 29 adenocarcinomas, and eight metastases. Distinct patterns of laminin-5 and integrin expression were found along the mucosa-adenoma, and adenoma-carcinoma transitions. Expression of basement membrane laminin-5 and subunits was continuous and gradient-like in normal mucosa, enhanced at the periphery of adenomas, and discontinuous

in places in carcinomas and metastases. Decrease of the alpha 3 integrin chain was found in adenomas, together with that of alpha 6 and beta 4 chains in carcinomas. A subpopulation of carcinoma cells dissociating (budding) from neoplastic tubules was found to accumulate the **laminin-5** beta 3 **gamma 2** heterodimer in the cytoplasm, with progressive loss of surface integrin expression. These results suggest that in colorectal cancer, an abnormal expression of laminin-5 subunits and integrin chains may identify a subset of carcinoma cells prone to invade focally and to contribute to disease aggressiveness.

L104 ANSWER 31 OF 38 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1997:28011895 BIOTECHNO
TITLE: Identification of cell binding sequences in mouse laminin chain by systematic peptide screening
AUTHOR: Nomizu M.; Kuratomi Y.; Song S.-Y.; Ponce M.L.; Hoffman M.P.; Powell S.K.; Miyoshi K.; Otaka A.; Kleinman H.K.; Yamada Y.
CORPORATE SOURCE: Y. Yamada, Craniofac. Devtl. Biol./Regen. Br, NIDR, NIH, Bethesda, MD 20892, United States.
E-mail: yamada@yoda.nidr.nih.gov
SOURCE: Journal of Biological Chemistry, (1997), 272/51 (32198-32205), 46 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Laminin-1, a major component of basement membranes, consists of three different chains designated .alpha.1, .beta.1, and .gamma.1 and has diverse biological functions. We have identified cell binding sites on the mouse laminin .gamma.1 chain, using systematic screening of 165 overlapping synthetic peptides covering the entire chain. We identified 12 cell binding Sequences using HT- 1080 human fibrosarcoma and B16-F10 mouse melanoma cells in two independent assays employing peptide-conjugated Sepharose beads and peptide-coated dishes. Four peptides (C-16, C-28, C-64, and C-68) located on the globular domains of the .gamma.1 chain were the most active and showed dose-dependent cell attachment. Cell attachment to C-68 was inhibited by EDTA and by anti-.alpha..sub.2.beta..sub.1 integrin **antibodies**. Cell attachment to C-16 and C-64 was partially inhibited by EDTA but was not inhibited by anti-integrin **antibodies**. EDTA and anti-integrin **antibodies** did not affect cell attachment to C-28. The four peptides were tested in adhesion and differentiation assays with endothelial, neuronal, and human salivary gland cells. C-16 was the most active for all of the cells, whereas the Other three peptides showed cell type specificity in their activities. The active core sequences of C-16, C-28, C-64, and C-68 are YVRL, IRVTLN, TTVKYIFR, and SIKIRGTY, respectively. These sequences are highly conserved among the different species and in the **laminin .gamma.2** chain. These results suggest that the specific sequences on the laminin .gamma.1 chain are biologically active and interact with distinct cell surface receptors.

L104 ANSWER 32 OF 38 CANCERLIT
ACCESSION NUMBER: 97360847 CANCERLIT
DOCUMENT NUMBER: 97360847
TITLE: Immunohistochemical analysis of the skin in junctional epidermolysis bullosa using **laminin 5** chain specific antibodies is of limited value in predicting the underlying gene mutation.

AUTHOR: McMillan J R; McGrath J A; Pulkkinen L; Kon A; Burgeson R E; Ortonne J P; Meneguzzi G; Uitto J; Eady R A
CORPORATE SOURCE: St John's Institute of Dermatology (UMDS), St Thomas' Hospital, London, U.K.
CONTRACT NUMBER: P01-AR38923 (NIAMS)
SOURCE: BRITISH JOURNAL OF DERMATOLOGY, (1997). Vol. 136, No. 6, pp. 817-22.
Journal code: AW0. ISSN: 0007-0963.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 97360847
ENTRY MONTH: 199709
AB The anchoring filament protein **laminin 5** is composed of three polypeptide chains (alpha 3, beta 3 and **gamma 2**) each encoded by separate genes (LAMA3, LAMB3 and LAMC2, respectively). Mutations in any of these three genes may give rise to the autosomal recessive blistering skin disease, junctional epidermolysis bullosa. At present, there is no easy way of predicting which of these three genes might harbour the pathogenetic **laminin 5** mutations in a case of junctional epidermolysis bullosa. In this study, we assessed whether immunohistochemistry might be helpful in this regard. We performed immunohistochemical labelling of the dermal-epidermal junction using alpha 3, beta 3 and **gamma 2** chain-specific antibodies in 11 patients with junctional epidermolysis bullosa, in whom the **laminin 5** mutations had been previously delineated. Although, labelling for the **laminin 5** chain bearing the mutations was attenuated or undetectable in all cases, a complete absence of labelling or a reduction in the staining intensity for the other two chains was also seen in all cases. The results showed that immunohistochemical labelling of the dermal-epidermal junction using alpha 3, beta 3 and **gamma 2** chain-specific antibodies is not a specific indicator for which of the **laminin 5** chain genes contains the pathogenetic mutations, and is therefore unreliable in screening for individual **laminin 5** gene mutations in cases of junctional epidermolysis bullosa.

L104 ANSWER 33 OF 38 CANCERLIT
ACCESSION NUMBER: 97247322 CANCERLIT
DOCUMENT NUMBER: 97247322
TITLE: Altered distribution and synthesis of laminin-5 (kalinin) in oral lichen planus, epithelial dysplasias and squamous cell carcinomas.
AUTHOR: Kainulainen T; Autio-Harmainen H; Oikarinen A; Salo S; Tryggvason K; Salo T
CORPORATE SOURCE: Oral and Maxillofacial Department, Oulu University Hospital, Finland.
SOURCE: BRITISH JOURNAL OF DERMATOLOGY, (1997). Vol. 136, No. 3, pp. 331-6.
Journal code: AW0. ISSN: 0007-0963.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 97247322
ENTRY MONTH: 199705
AB Laminin-5 is a glycoprotein which mediates epithelial cell adhesion to the basement membrane. This study describes the distribution and synthesis of laminin-5 in oral lichen planus, epithelial dysplasias, squamous cell carcinomas and a lymph node metastasis using immunohistochemistry and in situ hybridization. In normal oral mucosa and lichen planus,

immunoreaction to the laminin-5 was seen as a thin continuous, delicate line in the basement membrane region, although slight irregularities in the thickness and intensity of the immunoreaction could be detected in some cases with lichen planus. In epithelial dysplasias, the laminin-5 staining was discontinuous and more diffuse compared to lichen planus and normal mucosa. The immunoreaction was generally extracellular, although in some cases with lichen planus and epithelial dysplasia there were a few basal epithelial cells showing cytoplasmic staining. The invasive carcinomas and the lymph node metastasis showed a striking, intense cytoplasmic, staining of the carcinoma cells along the invasive border of the neoplastic islands and in individual infiltrating carcinoma cells. Using in situ hybridization, the **laminin-5 gamma 2** chain mRNA expression could not be detected in normal oral mucosa whereas, in non-dysplastic lichen planus and, more strongly, in dysplasias, there was a clear increase in the expression of laminin-5 mRNA in the basal epithelial cells. The most intensive signal was detected in the invasive front of the oral squamous cell carcinomas and the lymph node metastasis. We conclude that, in oral squamous cell carcinoma, there is altered synthesis and secretion of laminin-5 mRNA and protein. It is also evident that in dysplastic lesions of oral epithelium the synthesis and distribution of laminin-5 is abnormal.

L104 ANSWER 34 OF 38 CANCERLIT
ACCESSION NUMBER: 97191334 CANCERLIT
DOCUMENT NUMBER: 97191334
TITLE: Altered expression of the hemidesmosome-anchoring filament complex proteins in basal cell carcinoma: possible role in the origin of peritumoral lacunae.
AUTHOR: Bahadoran P; Perrin C; Aberdam D; Spadafora-Pisani A; Meneguzzi G; Ortonne J P
CORPORATE SOURCE: Department of Dermatology, Hopital Archetz, Nice, France.
SOURCE: BRITISH JOURNAL OF DERMATOLOGY, (1997). Vol. 136, No. 1, pp. 35-42.
Journal code: AW0. ISSN: 0007-0963.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 97191334
ENTRY MONTH: 199704

AB Basal cell carcinoma (BCC) is a frequent skin cancer with low metastatic potential. Expression of the anchoring filament proteins, native **laminin-5** and its individual alpha 3, beta 3 and **gamma 2** chains, uncein. and linear IgA antigen was examined by immunostaining in 17 BCC with different histological subtypes. Immunoreactivity of the hemidesmosomal proteins, integrin alpha 6 beta 4, 230-kDa bullous pemphigoid antigen (BP-230 Ag) and plectin/HD-1, and that of dermal-epidermal junction (DEJ) components, integrin alpha 2 beta 1, laminin-1, collagen IV, and collagen VII was also analysed. Around tumour nests, the labelling of **laminin-5** was absent or markedly reduced in 12 BCC (comprising eight solid BCC, three adenoid BCC and one keratotic BCC) and strong in five BCC (comprising three adenoid BCC, one keratotic BCC and one adenoid and keratotic BCC). Intriguingly, in tumour cells of 12 BCC including **laminin-5** negative tumours, a cytoplasmic reactivity of the laminin **gamma 2** chain was detected, but not that of the alpha 3 and beta 3 chains. In the basement membrane of the epidermis overlying tumour nests, the labelling of **laminin-5** was always strong. Uncein, linear IgA disease antigen, and integrin alpha 6 beta 4 were absent in solid BCC and weakly expressed in adenoid or keratotic BCC. For plectin/HD-1 and BP-230 Ag, a cytoplasmic reactivity was detected in the majority of the tumour

cells. The labelling of integrin alpha 2 beta 1, laminin-1, collagen IV and collagen VII indicated no alteration in the synthesis of these proteins. In peritumoral lacunae, immunoreactivity of hemidesmosome and anchoring filament proteins was absent, except for plectin/HD-1 on the tumour side and sometimes for **laminin-5** on the stromal side, while laminin-1, collagen IV and collagen VII were detected on the stromal side. These findings suggest that the components of the hemidesmosome-anchoring filament complex are not synthetized or assembled properly in BCC, and that the alteration of these adhesion structures may be the cause of peritumoral lacunae.

L104 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
ACCESSION NUMBER: 1996:377252 HCAPLUS
DOCUMENT NUMBER: 125:49293
TITLE: Human laminin 5 .gamma.2-chain antibody for diagnosis and antisense oligonucleotides for inhibition of malignant cell invasive growth
INVENTOR(S): Tryggvason, Karl; Kallunki, Pekka; Pyke, Charles
PATENT ASSIGNEE(S): Finland
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610646	A1	19960411	WO 1995-EP3918	19951004
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5660982	A	19970826	US 1994-317450	19941004
CA 2201865	AA	19960411	CA 1995-2201865	19951004
AU 9537451	A1	19960426	AU 1995-37451	19951004
AU 699183	B2	19981126		
EP 784703	A1	19970723	EP 1995-935428	19951004
EP 784703	B1	19990714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 182180	E	19990715	AT 1995-935428	19951004
ES 2133813	T3	19990916	ES 1995-935428	19951004

PRIORITY APPLN. INFO.: US 1994-317450 A 19941004
WO 1995-EP3918 W 19951004

AB The instant invention provides for the identification, diagnosis, monitoring, and treatment of malignant invasive cells using the laminin 5 .gamma.-2 chain protein or nucleic acid sequence, and antibodies or antisense oligonucleotides.

L104 ANSWER 36 OF 38 CANCERLIT
ACCESSION NUMBER: 97307459 CANCERLIT
DOCUMENT NUMBER: 97307459
TITLE: The integrin alpha 6 beta 4 and the biology of carcinoma.
AUTHOR: Rabinovitz I; Mercurio A M
CORPORATE SOURCE: Beth Israel Hospital, Boston, MA, USA.
SOURCE: BIOCHEMISTRY AND CELL BIOLOGY, (1996). Vol. 74, No. 6, pp. 811-21.

Journal code: ALR. ISSN: 0829-8211.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 97307459
ENTRY MONTH: 199708

AB The integrin family of adhesion receptors plays a major role in epithelial organization and function. Moreover, the altered expression and function of specific integrins most likely contributes significantly to carcinoma progression. The integrin alpha 6 beta 4, the focus of this review, is a receptor for several members of the laminin family and is preferentially expressed at the basal surface of most epithelia, where it contributes to basement membrane interactions. Mounting evidence suggests that the alpha 6 beta 4 integrin plays a key role in carcinoma cell biology. Several histopathological studies have established a correlation between alpha 6 beta 4 integrin expression and tumor progression. The importance of alpha 6 beta 4 expression in tumors in underscored by the findings that invading fronts of several carcinomas are enriched in the expression of alpha 6 beta 4 integrin ligands, such as laminin-1 and **laminin-5** . The participation of the alpha 6 beta 4 integrin in invasion is supported further by in vitro functional studies using carcinoma cells that have been transfected with the beta 4 cDNA. The mechanisms by which alpha 6 beta 4 contributes to tumor progression are probably related to its mechanical and signaling properties and are currently under intense study.

L104 ANSWER 37 OF 38 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
ACCESSION NUMBER: 1995:25274977 BIOTECHNO
TITLE: Laminin-5 is a marker of **invading** **cancer** cells in some human carcinomas and is coexpressed with the receptor for urokinase plasminogen activator in budding **cancer** cells in colon adenocarcinomas
AUTHOR: Pyke C.; Salo S.; Ralfkiaer E.; Romer J.; Dano K.; Tryggvason K.
CORPORATE SOURCE: Finsen Laboratory, Righospitalet, Strandboulevarden 49,DK-2100 Copenhagen, Denmark.
SOURCE: Cancer Research, (1995), 55/18 (4132-4139)
CODEN: CNREA8 ISSN: 0008-5472
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Recombinant human .**gamma**.2 chain of **laminin** **-5** was expressed in Escherichia coli, and used to generate specific polyclonal **antibodies** which were used to study the distribution of the protein in human **cancers**. A total of 72 biopsies of human **cancers** were stained, including 23 cases of colon adenocarcinomas, 16 ductal breast carcinomas, 9 malignant melanomas, 14 squamous cell carcinomas of the skin and cervix, and 10 **sarcomas**. As a control for the specificity of the **antibodies**, we performed in situ hybridization on adjacent sections of a number of the cases, and in all of these cases the localization of the .gamma.2 chain protein and mRNA was identical. We found .gamma.2 chain immunoreactivity in **cancer** cells in all cases of colon adenocarcinomas and squamous cell carcinomas but not in any of the **sarcomas**, supporting the view that the laminin-5 protein is specific for cells of epithelial origin. Notably, in all of

the cases of colon adenocarcinomas, the positive staining was invariably associated with budding **cancer** cells located at the tip of **invading** malignant epithelium, whereas the **cancer** cells deeper in the **tumors** were most often negative. The staining was cytoplasmic in all cases and only in one case did we see additional extracellular immunoreactivity, indicating that this laminin isoform in **cancer** tissue is not laid down in the extracellular matrix but probably exerts its function at the cell surface or in its immediate vicinity. Using in situ hybridization to analyze the coexpression of laminin-5 and components of the plasminogen activation system, we found that the histological distribution of laminin-5- positive budding **cancer** cells at the **invasion** front in colon adenocarcinomas was identical to that of the receptor for urokinase-type plasminogen activator. These findings suggest that laminin-5 is a marker of **invading cancer** cells in at least some human malignancies, and that it therefore might represent a valuable marker for the **invasive** potential of these **cancers**. The colocalization of laminin-5 and urokinase-type plasminogen activator receptor in a subset of **cancer** cells in colon **cancer** also suggests that a controlled up-regulation of a number of gene products is a characteristic budding colon **cancer** cells, and that these gene products serve functions crucial for the **invasive** phenotype of these **cancer** cells.

L104 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:9049 HCAPLUS
DOCUMENT NUMBER: 124:84388
TITLE: .gamma.2 Chain of laminin-5 is recognized by monoclonal antibody GB3
AUTHOR(S): Matsui, Chihiro; Nelson, Charlotte F.; Hernandez, German T.; Herron, G. Scott; Bauer, Eugene A.; Hoeffler, Warren K.
CORPORATE SOURCE: School Medicine, Stanford University, Stanford, CA, 94305, USA
SOURCE: J. Invest. Dermatol. (1995), 105(5), 648-52
CODEN: JIDEAE; ISSN: 0022-202X
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AB Herlitz junctional epidermolysis bullosa is an autosomal recessive disorder characterized by generalized blistering at the lamina lucida of the cutaneous basement membrane. The monoclonal antibody GB3 has been used as a diagnostic probe because of its lack of reactivity in patient skin. The antigen recognized by GB3 has been identified as laminin-5, a glycoprotein consisting of three subunits (.alpha.3, .beta.3 and .gamma.2). To identify the laminin-5 protein chain that contains the epitope recognized by GB3 and to det. if chain assembly is required for antibody recognition, the authors expressed a .gamma.2 protein constructed from a full-length .gamma.2 cDNA. Radioimmunopptn. of the culture medium from 293 cells revealed that both GB3 and anti-.gamma.2 polyclonal antibodies were capable of directly pptg. recombinant .gamma.2 without copptn. of other proteins. In immunodepletion expts., each antibody removed most of the protein that was reactive with the other antibody. The epitope recognized by GB3 is present only when the complex is in the native conformation because GB3 reacted only with the non-reduced laminin-5, but not the reduced laminin-5 in immunoblots. Moreover, because GB3 reacted with laminin-5 of SCC25 cells (.gamma.2 in the heterotrimer) but not recombinant .gamma.2 in 293 cells (.gamma.2 alone) during indirect immunofluorescence staining, this epitope may be dependent upon a less stable conformation of .gamma.2. The authors conclude that GB3 recognizes the .gamma.2 chain of laminin-5 and that the epitope is

entirely contained in the native form of the .gamma.2 chain.